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(88) Date of publication of the international search report: 11 August 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: RNA INTERFERENCE MEDIATED TREATMENT OF PARKINSON DISEASE USING SHORT INTERERING NUCLEIC ACID (siNA)

(57) Abstract: The present invention concerns methods and reagents useful in modulating Parkinson genes, for example, PARK1 (SNCA), PARK2, PARK7, and/or PARK5 gene expression in a variety of applications, including use in therapeutic, diagnostic, target validation, and genomic discovery applications. Specifically, the invention relates to small nucleic acid molecules, such as short interfering nucleic acid (siNA), short interfering RNA (siRNA), double-stranded RNA (dsRNA), micro-RNA (miRNA), and short hairpin RNA (shRNA) molecules capable of mediating RNA interference (RNAi) against SNCA gene expression and/or activity. The small nucleic acid molecules are useful in the diagnosis and treatment of Parkinson Disease (PD), and any other disease or condition that responds to modulation of PARK1 (SNCA), PARK2, PARK7, and/or PARK5 expression or activity.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/017630

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/11 C12P19/34 C07H21/02 C07H21/04 A01N43/04
A61K31/713

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, EMBASE, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/49844 A (DRISCOLL MONICA ; UNIV RUTGERS (US); TAVERNARAKIS NEKTARIOS (US)) 12 July 2001 (2001-07-12) page 11, lines 6-15 page 45, line 34 - page 46, line 2	1,3-11, 23,28, 29,31, 32,34
Y		2,12-22, 24-27,30
Y	WO 03/070918 A (MOKLER VICTOR ; FOSNAUGH KATHY (US); JAMISON SHARON (US); MACEJAK DENN) 28 August 2003 (2003-08-28) page 6, line 11 - page 14, line 17	2,12-22, 24-27,30

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 January 2005	13. 06. 2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Barnas, C

Form PCT/ISA/210 (second sheet) (January 2004)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	NELSON P T ET AL: "The mRNA of alpha-synuclein is a putative microRNA (miRNA) target." SOCIETY FOR NEUROSCIENCE ABSTRACT VIEWER AND ITINERARY PLANNER, vol. 2003, 2003, pages Abstract No. 558.8 URL-http://sf, XP001181837 & 33RD ANNUAL MEETING OF THE SOCIETY OF NEUROSCIENCE; NEW ORLEANS, LA, USA; NOVEMBER 08-12, 2003 abstract	1,3-9, 23,28, 29,31, 32,34
P,X	SAPRU M K ET AL: "Small interfering RNA (SiRNA) - mediated silencing ofalpha - synuclein gene expression." SOCIETY FOR NEUROSCIENCE ABSTRACT VIEWER AND ITINERARY PLANNER, vol. 2003, 2003, pages Abstract No. 297.9 URL-http://sf, XP001204566 & 33RD ANNUAL MEETING OF THE SOCIETY OF NEUROSCIENCE; NEW ORLEANS, LA, USA; NOVEMBER 08-12, 2003 abstract	1,3-9, 23,28, 29,31, 32,34
P,X	WO 03/099298 A (MAX PLANCK GESELLSCHAFT ; TUSCHL THOMAS (DE); ELBASHIR SAYDA (DE); LEN) 4 December 2003 (2003-12-04) page 20, lines 29,30	1,3-9, 23,28, 29,31, 32,34
E	WO 2004/047872 A (MEDTRONIC INC) 10 June 2004 (2004-06-10) page 6, lines 5-11	1-32,34

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/017630

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-32, 34

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-32, 34

A double stranded short interfering nucleic acid (siNA) molecule that directs cleavage of an alpha-synuclein (SNCA) RNA via RNA interference as described in claim 1.

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2. claims: 1, 33, 35 (part)

A double stranded short interfering nucleic acid (siNA) molecule that directs cleavage of an alpha-synuclein (SNCA) RNA via RNA interference as described in claim 1 wherein said siNA comprises any of SEQ ID NOs: 1-30, 87-116.

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3. claims: 1, 33, 35 (part)

A double stranded short interfering nucleic acid (siNA) molecule that directs cleavage of an alpha-synuclein (SNCA) RNA via RNA interference as described in claim 1 wherein said siNA comprises any of SEQ ID NOs: 31-60, 117-146.

---

4. claims: 1, 33, 35 (part)

A double stranded short interfering nucleic acid (siNA) molecule that directs cleavage of an alpha-synuclein (SNCA) RNA via RNA interference as described in claim 1 wherein said siNA comprises any of SEQ ID NOs: 61-86, 147-172.

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5. claims: 1, 33, 35 (part)

A double stranded short interfering nucleic acid (siNA) molecule that directs cleavage of an alpha-synuclein (SNCA) RNA via RNA interference as described in claim 1 wherein said siNA comprises any of SEQ ID NOs:173-210, 211-248.

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6. claims: 1, 33, 35 (part)

A double stranded short interfering nucleic acid (siNA) molecule that directs cleavage of an alpha-synuclein (SNCA) RNA via RNA interference as described in claim 1 wherein said siNA comprises any of SEQ ID NOs: 249-370.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/017630

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